SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

SUMMARY OF SAFETY AND EFFECTIVENESS DATA
FOR A SUPPLEMENTAL PREMARKET APPROVAL APPLICATION

I. GENERAL INFORMATION

Device Generic Name:	Ophthalmic Excimer Laser System
Device Trade Name:	VISX STAR S4 IR™ Excimer Laser System with Variable Spot Scanning (VSS™) and WaveScan WaveFront® System
Applicant's Name and Address:	VISX, Incorporated 3400 Central Expressway Santa Clara, CA 95051-0703
Date of Panel Recommendation:	None
Premarket Approval (PMA) Application Number:	P930016/S020
Date of Notice of Approval to Applicant:	

The STAR Excimer Laser was originally approved on March 27, 1996, under PMA P930016, for the limited indication for myopic photorefractive keratectomy (PRK) using a 6.0 mm ablation zone in patients 18 years of age or older with 1.0 to 6.0 diopters (D) of myopia with astigmatism of ≤ 1.0 D whose refractive change for one year prior to treatment is within ± 0.5 D.

This clinical indication was expanded in supplements 3 (approved on April 24, 1997), 5 (approved on January 29, 1998), 7 (approved November 2, 1998), and 10 (approved October 18, 2000) to include PRK in patients 21 years of age or older in PRK treatments for the reduction or elimination of myopia (nearsightedness) of between 0 and -12.0 D spherical myopia at the spectacle plane and up to -4.0 D of astigmatism, hyperopia (sphere only) of between +1.0 and +6.0 D spherical equivalent with no more than 1.0 D of refractive astigmatism, and hyperopia between +0.5 and +5.0 D sphere at the spectacle plane with refractive astigmatism from +0.5 to +4.0 D with a maximum manifest refraction spherical equivalent (MRSE) of +6.0 D. On November 19, 1999 (P990010), the clinical indication was further expanded to include laser in situ keratomileusis (LASIK) treatments in patients 18 years of age or older for the reduction or elimination of myopia (nearsightedness) from 0 to -14.0 D with or without -0.50 to -5.0 D of astigmatism. Supplement 12 (approved April 27, 2001) expanded the indication to include patients 21 years of age or older in treatments for the reduction or elimination of naturally occurring hyperopia between +0.5 D and +5.0 D sphere at the spectacle plane with or without refractive astigmatism up to +3.0 D with a maximum manifest refraction spherical equivalent (MRSE) of +6.0 D. Supplement 14 (approved November 16, 2001) expanded the indication for the reduction or elimination of naturally occurring mixed astigmatism where the magnitude of cylinder (≤ 6.0 D at the spectacle plane) is greater than the magnitude of sphere and the cylinder and sphere have opposite signs. Supplement 15 (approved August 7, 2002) added an auto-centering function to the ActiveTrak™ eye tracking system and changed the trade name to the STAR S4. Supplement 16 (approved May 23, 2003) expanded the clinical indication for wavefront-guided laser assisted in situ keratomileusis (LASIK) for the reduction or elimination of myopic astigmatism up to - 6.00 D MRSE, with cylinder between 0.00 and -3.00 D. Supplement 18 (approved June 7, 2004) introduced the Fourier Transform Analysis of Hartmann-Shack data in WaveScan Version 3.50. Supplement 17 (approved December 14, 2004) expanded the clinical indication for wavefront-guided laser assisted in situ keratomileusis (LASIK) for the reduction or elimination of hyperopic astigmatism

up to 3.00 D MRSE, with cylinder between 0.00 and 2.00 D. Supplement 19 (approved February 18, 2005) added an iris identification and registration system, an ozone compensation system, and changed the trade name to the STAR S4-IR Excimer Laser System.

The sponsor submitted this supplement to further expand the clinical indications to include wavefront-guided mixed astigmatism. The updated clinical data to support the expanded indication is provided in this summary. For more information on the data which supported the approved indications, the summaries of safety and effectiveness data (SSED) for P930016 and P990010 should be referenced. Written requests for copies of the SSED can be obtained from the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20857 under Docket # 97M-0084 (P930016 and S3), Docket # 99M-0293 (S5), Docket # 00M-1391 (S7), Docket # 01M-0015 (S10), Docket # 01M-0305 (S12), Docket # 01M-0522 (S14), Docket # 03M-0333 (S16), Docket # 05M-0055 (S17) and Docket # 00M-1447 (P990010) or you may download the files from the internet sites http://www.fda.gov/cdrh/pdf/p930016.pdf and http://www.fda.gov/cdrh/pdf/p990010.pdf.

II. INDICATIONS FOR USE

The STAR S4 IR™ Excimer Laser System with Variable Spot Scanning (VSS™) and the WaveScan® System is indicated for wavefront-guided laser assisted in situ keratomileusis (LASIK):

- for the reduction or elimination of naturally occurring mixed astigmatism when the magnitude of cylinder (from 1.0 to 5.0 D) is greater than the magnitude of sphere and the cylinder and sphere have opposite signs;
- in patients 21 years of age or older; and
- in patients with documented evidence of a change in manifest refraction of no more than 0.50 D (in both cylinder and sphere components) for at least one year prior to the date of pre-operative examination.

III. CONTRAINDICATIONS

Laser refractive surgery is contraindicated:

- in patients with collagen vascular, autoimmune or immunodeficiency diseases.
- in pregnant or nursing women.
- in patients with signs of keratoconus or abnormal corneal topography
- in patients who are taking one or both of the following medications: isotretinoin (Accutane®) or amiodarone hydrochloride (Cordarone®).

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the device labeling.

V. DEVICE DESCRIPTION

A. WaveScan WaveFront® System

The WaveScan WaveFront System is an integral part of this approval. It is a class III accessory device and has a separate user manual. It is a diagnostic instrument indicated for the automated measurement, analysis, and recording of refractive errors of the eye: including myopia, hyperopia, astigmatism, coma, spherical aberration, trefoil, and other higher order aberrations through sixth order, and for displaying refractive data of the eye to assist in prescribing refractive correction.

The WaveScan WaveFront System measures the refractive error and wavefront aberrations of the human eye using a Hartmann-Shack wavefront sensor. The measurements can be used to determine regular (sphero-cylindrical) refractive errors and irregularities (aberrations) that cause decreased or blurry vision in the human eye.

The function of the Hartmann-Shack sensor is to measure the refractive error of the eye by evaluating the deflection of rays emanating from a small beam of light projected onto the retina. To control the natural accommodation of the eye during WaveScan® imaging, the system incorporates a fogged fixation target.

The WaveScan System optical head projects a beam of light onto the retina. The light reflects back through the optical path of the eye and into the wavefront device. The reflected beam is imaged by a lenslet array onto the charge-coupled device (CCD). Each lens of the array gathers light information (deflection information) from a different region of the pupil to form an image of the light that passes through that region of the pupil. An array of spots are imaged on the CCD sensor. The system compares the locations of the array of spots gathered from the CCD to the theoretical ideal (the ideal plane wave).

The WaveScan System software uses these data to compute the eye's refractive errors and wavefront aberrations using Fourier Transform analysis. The system displays the refractive errors and wavefront aberrations as the optical path difference (OPD) between the measured outgoing wavefront and the ideal plane wave. The WaveScan system software subtracts the refractive errors from the wavefront errors map and displays the higher order aberrations as OPD errors. Regions of the pupil with positive OPD are in front of the ideal plane wave and areas with negative OPD are behind the ideal plane wave.

1. Data Collection

   The eye of the patient is centered in the instruments field of view and the image of the eye is brought in focus. As the patient fixates on the target, the fogging system is engaged to optically adjust the position of the target beyond the far point of the patient. This forces the patient to relax their accommodative system, so that the refraction of the eye is measured accurately. There is no pharmaceutical eye dilation required for the patient.

2. Wavefront Measurement

   During the data capture, four images are captured from the Hartmann-Shack camera within a short interval of time. The pupil camera of the instrument captures the image of the eye during the same time interval. The spot pattern images are processed to

reconstruct the wavefront and if two or more of them pass the acceptance criteria, the valid measurements are averaged to yield the final measurement for the examination.

3. Registration

   Internal instrument calibration establishes the coordinate transformation between the pupil imaging camera and the Hartmann-Shack camera, so that the wavefront map can be correctly centered at the center of the pupil during the measurement.

4. Treatment Design

   The target treatment shape is automatically calculated by the WaveScan instrument from the wavefront data. Once the target shape is established, VSS™ software module generates the commands for the laser to create the target shape on the cornea. Corneal geometry, represented by the keratometry values, is taken into account in computing the laser instructions.

   CustomVue™ ablations for mixed astigmatism are approved for an optical zone of 6.0 mm, and an ablation zone of 9.0 mm. No treatments with optical zones greater than 6.0 mm were attempted in the U.S. Clinical Trial. All treatments utilized a variable repetition rate to a maximum of 20 Hz. CustomVue ablations for this PMA are locked out above 5.0 D cylinder as measured by manifest refraction.

   The final commercial release versions for CustomVue are WaveScan software version 3.62 together with STAR software version 5.0. The WaveScan software is capable of calculating mixed astigmatism treatments with an optical zone up to 6.5 mm with total ablation zone up to 9.5 mm.

5. Data Transfer

   The treatment files produced by the WaveScan® instrument contain information about the patient, such as name, ID and refractive data, iris image, and the set of instructions for the VISX STAR laser. They are copied onto a USB flash drive or floppy disk for transfer to the laser. The files are encrypted to prevent data tampering or data corruption.

Features and components of the WaveScan WaveFront System include:

- Computer Control
- PC and Monitor
- Isolation Transformer
- Power Supply
- LED
- Optical Head
- Printer
- Motorized table

B. Microkeratome

The LASIK procedure required the use of a commercially available microkeratome that has been cleared for marketing via premarket notification. Three different microkeratomes were used in this study. Each device consisted of a sterilization/storage tray which includes the shaper head, a left/right eye adapter, suction ring, suction handle, blade handling pin, and corneal reference marker. The instrument motor, tonometer, cleaning brush, disposable blades, power/suction supply unit with vacuum and motor footswitches and power cords are provided as separate components in an accessory stand and equipment suitcase which complete the system.

C. STAR S4 IR™ Excimer Laser System

The STAR S4 IR laser system is a 193 nm excimer laser system that delivers spatially scanning ultraviolet pulses of variable diameters and slits on to the cornea. The range of diameters and slits available during treatments are 0.65 mm to 6 mm. An auto-centering dual camera infrared eye tracking system (ActiveTrak™), together with the delivery system, aligns the treatment to the eye and compensates for eye movements during laser correction to maximize the corneal reshaping accuracy. An operating microscope is used to observe the patient procedures and to facilitate accurate focus and laser beam alignment. A debris-removal system is designed to evacuate the debris plume that occurs during ablation. The operating chair and fixation LED align the patient, while a video camera and monitor records the patient treatment.

The variable spot scanning (VSS™) feature of the laser, used for CustomVue™ treatments delivers variable diameter ultraviolet pulses to precise locations by the scanning delivery system. The VSS algorithm optimizes the ablation pattern by choosing the best combination of beam diameters and locations to achieve a target shape. VSS expands the laser capability to achieve a broader spectrum of ablation shapes than conventional treatments because the conventional algorithm optimizes only the diameter for myopic treatments and slits for hyperopic treatments.

Conventional STAR treatments utilize sphere, cylinder and axis components which are entered manually into the laser by the operator to generate the ablation treatment. CustomVue™ treatment information is generated on the WaveScan® system and transferred to the STAR S4 IR Excimer Laser System. The transferred information includes patient information, eye and refraction information, image of the eye, eye alignment information, and ablation instructions to the laser for beam diameters and the exact locations of the beam on the cornea. The VISX Treatment card defines the number and the types of treatments available.

Wavefront-guided treatments using the STAR S4 IR™ and WaveScan Systems utilize an automated iris identification and registration system. The angle of rotation of the patient's eye under the laser is determined by comparing features of the iris on the WaveScan image to the same features located in the image of the iris taken using the STAR S4 IR camera. The treatment is rotated to align precisely with the rotation of the patient's eye under the laser.

The STAR S4 IR laser software also contains a refinement to the method of STAR laser beam energy control by inclusion of an ozone compensation system.

Features and components of the STAR S4 IR System include:

- Excimer Laser
- Gas Management System

- Laser Beam Delivery System
- Patient Management System
- Computer Control
- VISX Treatment Card

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are currently several other alternatives for the correction of mixed astigmatism:

- Automated lamellar keratoplasty (ALK)
- Contact Lenses
- Conventional Laser in-situ keratomileusis (LASIK - based on phoropter refraction)
- Conventional Photorefractive Keratectomy (PRK - based on phoropter refraction)
- Radial Keratotomy (RK)
- Spectacles

Each alternative has its own advantages and disadvantages. A prospective patient should fully discuss with his/her care provider these alternatives in order to select the correction method that best meets his/her expectation and lifestyle.

VII. MARKETING HISTORY

The VISX STAR™ Excimer Laser System has been distributed in 62 countries (Argentina, Aruba, Austria, Australia, Belgium, Bolivia, Brazil, Bulgaria, Canada, Chile, China, Colombia, Cyprus, Czech Republic, Dijibouti, Dominican Republic, Dubai, Ecuador, Egypt, Finland, France, Germany, Greece, Guatemala, Hong Kong, Hungary, Indonesia, India, Ireland, Israel, Italy, Jamaica, Japan, Korea, Kuwait, Mexico, The Netherlands, New Zealand, Norway, Pakistan, Paraguay, Peru, Philippines, Portugal, Romania, Russia, Russia-Kazakhstan, Saudi Arabia, Singapore, Slovak Republic, Spain, Sweden, Switzerland, Taiwan, Thailand, Turkey, Ukraine, United Kingdom, the United States, Uruguay, Venezuela and Vietnam). The VISX STAR Excimer Laser System has not been withdrawn from any country or market for reasons of safety or effectiveness.

The WaveScan WaveFront® System has been distributed in approximately 44 countries (Argentina, Aruba, Australia, Austria, Brazil, Bulgaria, Canada, Chile, China, Colombia, Cyprus, Czech Republic, Dominican Republic, Egypt, Finland, France, Germany, Greece, India, Indonesia, Ireland, Israel, Italy, Japan, Korea, Kuwait, Mexico, The Netherlands, Philippines, Portugal, Russia, Saudi Arabia, Singapore, Spain, Sweden, Taiwan, Thailand, Turkey, UAE, Ukraine, United Kingdom, the United States, Uruguay and Vietnam). The WaveScan WaveFront System has not been withdrawn from any country or market for reasons of safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse reactions associated with LASIK include: loss of best spectacle corrected visual acuity (BSCVA), worsening of patient complaints such as double vision, sensitivity to bright lights, increased difficulty with night vision, fluctuations in vision, increase in intraocular pressure, corneal haze, secondary surgical intervention, corneal infiltrate or ulcer, corneal epithelial defect,

corneal edema, problems associated with the flap including a lost, misplaced or misaligned flap, retinal detachment, and retinal vascular accidents.

Please refer to the complete listing of adverse events and complications observed during the clinical study which are presented on pages 20 and 21 of the clinical study section.

IX. SUMMARY OF PRECLINICAL STUDIES

A. STAR™ Excimer Laser System

For a summary of non-clinical studies (excluding hazard analysis and software testing) for the STAR Excimer Laser System, refer to the SSED of the original PMA #P930016.

B. WaveScan Wavefront® System

1. Hazard Analysis

   Hazard Analysis and Software Testing was conducted for the combined use of the WaveScan WaveFront System and the STAR Excimer Laser System. Hazard Analysis includes 3 separate fault tree analyses (FTAs): WaveScan 3.62, Topographer Measurement for Custom Contoured Ablation Patterns Method (C-CAP) Treatments and STAR software 5.0 version with C-CAP and WavePrint treatment. The WaveScan FTA encompasses the process from patient measurement to the generation of treatment table files. The Topographer FTA encompasses the process from patient measurement to treatment printout. The STAR FTA encompasses all previously identified fault and mitigating circumstances identified with any given treatment process. The software test procedures covered all aspects of new software functionality and performance. All test procedures were completed. The Hazard Analysis and software test report indicated no new hazards affecting safety or effectiveness.

2. Testing for Measurement of Refractive Errors of the Eye with WaveScan Wavefront System

   A bench top study for the measurement of total refractive errors of the eye, including myopia, astigmatism, coma, spherical aberrations, trefoil and other higher order aberrations through sixth order, and Software Testing was conducted for the WaveScan WaveFront® System. The test was designed to measure conventional aberrations in a VISX model eye and in 8 phase plates with different combinations of Zernike aberrations. The data from this study indicated the VISX WaveScan WaveFront System provides an adequate and reliable measurement of total refractive errors of the eye, including myopia, astigmatism, coma, spherical aberration, trefoil and other higher order aberration through sixth order.

3. Profilometry of Ablation

   As a part of this PMA, VISX validated the accuracy of WaveScan-derived mixed astigmatism corrections by performing test ablations on plastic surfaces. All ablations were scanned with a surface profilometer and showed very good agreement to theoretical targets.

X. SUMMARY OF CLINICAL STUDIES

A clinical study of LASIK treatment, with the VISX STAR S4 IR™ Excimer Laser System with Variable Spot Scanning and WaveScan-derived ablation targets for the correction of mixed astigmatism, was conducted under IDE G010048. The data from this study are presented as a basis for consideration and approval. Specifically, safety and effectiveness outcomes at 3 months postoperatively were assessed as stability is reached by that time. The IDE study is described in detail as follows:

A. Study Objective

The objective of this clinical investigation was to demonstrate that LASIK treatment with the VISX STAR Excimer Laser System with Variable Spot Scanning and WaveScan derived ablation targets is safe and effective for the correction of mixed astigmatism.

B. Study Design

This was a prospective, multi-center, open-label, non-randomized study where the primary control was the preoperative state of the treated eye (i.e., comparison of pretreatment and post-treatment visual parameters in the same eye).

C. Inclusion and Exclusion Criteria

Enrollment in the study on the effect of LASIK treatment with the VISX STAR Excimer Laser System using Variable Spot Scanning technology with WaveScan® derived ablation targets, was limited to those subjects who met the following inclusion criteria in their operative eye(s):

- Male or female subjects of any race, and at least 21 years old at the time of the pre-operative examination.
- Uncorrected distance visual acuity (UCVA) of 20/40 or worse.
- Mixed astigmatism: magnitude of cylinder ($\leq$ 5.0 D at the spectacle plane) is greater than the magnitude of sphere and the sphere and cylinder have opposite signs; and manifest spherical equivalent (MRSE) $\geq$ 1.00 D and/or cylinder component $\geq$ 1.00 D.
- Best spectacle corrected visual acuity (BSCVA) of 20/25 or better.
- Wavefront measurement diameter $\geq$ 5.0 mm.
- Manifest refraction within ± 0.75D of WaveScan refraction (sphere and cylinder) and no more than 15 degrees of difference between axes for eyes with cylinder greater than 0.50 D.
- Manifest refraction within ± 0.75 D of Cycloplegic refraction (sphere and cylinder) and no more than 15 degrees of difference between axes for eyes with cylinder greater than 0.50 D.
- WaveScan refraction within ± 0.75 D of Cycloplegic refraction (sphere and cylinder) and no more than 15 degrees of difference between axes for eyes with cylinder greater than 0.50 D.

- Pachymetric measurement minus the maximal depth ablated (as described by the VISX software) added to the flap thickness is greater than or equal to 250 microns (i.e., Pachymetry – [Depth of ablation + Flap thickness] ≥ 250 microns).

- Eyes that demonstrated refractive stability confirmed by a change of less than or equal to 1.0 diopter (sphere and cylinder) at an exam at least 12 months prior to the baseline examination. The astigmatic axis must also be within 15 degrees for eyes with cylinder greater than 0.50 D.

- Contact lens wearers who removed soft lenses at least 1 week prior and rigid (Gas permeable and PMMA) lenses at least 2 weeks prior to baseline measurements. At that baseline examination, cycloplegic and manifest refractions as well as corneal topography were obtained. If the investigator determined that the topography was within normal limits, surgery was scheduled at least one week after the initial exam, with no contact lens wear permitted prior to the surgery. If on the day of scheduled surgery, for the operative eye, repeat central keratometry readings and manifest refraction spherical equivalents did not differ significantly from the initial exam measurements (by more than 0.50 diopter), surgery proceeded. If the refractive change exceeded this criterion, the surgery was rescheduled after refractive stability was achieved.

- Planned treatment such that the anticipated post-operative keratometry value in any meridian will be ≤ 50 D. Anticipated post-operative keratometry values will be calculated by: a) adding the total amount of pre-operative manifest sphere and cylinder to the power of the keratometry value in the flat meridian (i.e., sphere (D) + cylinder (D) + Flat K), and b) adding the total amount of pre-operative manifest sphere to the power of the keratometry value in the steep meridian, (i.e., sphere (D) + Steep K).

- Subjects willing and capable of returning for follow-up examinations for the duration of the study.

Patients were not permitted to enroll in the study if they met any of the following exclusion criteria:

- Female subjects who were pregnant, breast-feeding or intended to become pregnant over the course of the study.

- Subjects whose fellow eye did not meet all inclusion criteria or fall within approved indications for treatment using the VISX STAR Excimer Laser.

- Subjects who used concurrent topical or systemic medications which might have impaired healing, including but not limited to: antimetabolites, isotretinoin (Accutane®) within 6 months of treatment, and amiodarone hydrochloride (Cordarone®) within 12 months of treatment.

NOTE: The use of topical or systemic corticosteroids, whether chronic or acute, was deemed to adversely affect healing and subjects using such medication were specifically excluded from eligibility.

- Subjects who had a history of any of the following medical conditions, or any other condition that could have affected wound healing: collagen vascular disease, autoimmune disease, immunodeficiency diseases, ocular herpes zoster or simplex,

endocrine disorders (including, but not limited to unstable thyroid disorders and diabetes), lupus, and rheumatoid arthritis.

NOTE: The presence of diabetes (either type 1 or 2), regardless of disease duration, severity or control, specifically excluded subjects from eligibility.

- Subjects who had a history of prior intraocular or corneal surgery (including cataract extraction), active ophthalmic disease or abnormality (including, but not limited to, blepharitis, recurrent corneal erosion, dry eye syndrome, neovascularization > 1mm from limbus), clinically significant lens opacity, clinical evidence of trauma (including scarring), at risk for developing strabismus, evidence of glaucoma, or propensity for narrow angle glaucoma in the operative eye(s).

NOTE: This included any subject with open angle glaucoma, regardless of medication regimen or control. Additionally, any subject with an IOP greater than 21 mm Hg at baseline was specifically excluded from eligibility.

- Subjects who had evidence of keratoconus, corneal irregularity, or abnormal videokeratography in the operative eye(s).

- Subjects who had known sensitivity or inappropriate responsiveness to any of the medications used in the post-operative course.

- Subjects who were participating in any other clinical trial.

D. Study Plan, Patient Assessments, and Efficacy Criteria

All subjects were expected to return for follow-up examinations at 1 and 7 days, and 1, 3, 6, 9, 12 and 24 months postoperatively.

Subjects were permitted to have second eyes (fellow eyes) treated at the discretion of the investigator at the same time as the first eye (primary eyes) or after the primary eye treatment.

In addition, subjects were eligible for retreatment no sooner than 3 months after treatment with submission of appropriate clinical data, planned treatment, and agreement of the medical monitor in advance. To qualify for retreatment, stability of the refractive outcome must have been documented with serial topographies taken at least 4 weeks apart showing less than 1.0 D of corneal power change in the treatment area, or with manifest refractions taken at least 4 weeks apart showing less than 1.0 D of variation in the manifest refraction spherical equivalent. Refractive retreatments could be performed if the subject met at least one of the following criteria:

- Manifest refractive spherical equivalent of 0.5 D or greater;

- Manifest astigmatism of 0.5 D or more;

- Distance uncorrected visual acuity of 20/32 or worse; or

- Subjective complaints by the patient with treatable cause as determined by the investigator

At this time, 6 eyes underwent retreatment in the study.

All study treatments were conducted using a 6 mm optical zone and a 9 mm ablation zone with intention of full correction to emmetropia.

The parameters measured during the study were:

- At 1 and 3 months: visual acuity (uncorrected, uncorrected near, distance corrected near, and best spectacle corrected), manifest refraction, keratometry, videokeratography, WaveScan® measurement, contrast sensitivity, applanation tonometry, anterior segment examination by biomicroscopy, and a subjective questionnaire. Dim pupil size was also conducted on each patient at the 3-month visit only. Adverse events, complications, medications and other clinical findings were also noted.

Additional parameters to be measured during the study were:

- At 6, 9, 12, and 24 months: visual acuity (uncorrected, uncorrected near, distance corrected near, and best spectacle corrected), manifest refraction, keratometry, corneal videokeratography, WaveScan measurement, contrast sensitivity, applanation tonometry, anterior segment examination by biomicroscopy, and a subjective questionnaire. After cycloplegia, a refraction, dilated media and fundoscopic examination were performed. Adverse events, complications, medications, and other clinical findings were noted as appropriate. If 12 and 24-month examinations are necessary, uncorrected near visual acuity, distance corrected near visual acuity, contrast sensitivity, cycloplegic refraction, dilated fundus examination. and a patient questionnaire are required.

- The primary efficacy variables for this study were: improvement of UCVA, predictability of manifest cylinder, and refractive stability.

E. Study Period, Investigational Sites, and Demographics

1. Study Period and Investigational Sites

Forty-four (44) subjects were treated between May 13, 2003 and November 11, 2003. The database for this PMA supplement reflected data collected through November 10, 2004 and included 86 eyes. There were 6 investigational sites that provided eligible data for analysis.

2. Demographics

Of the 86 treated eyes, 66% (57/86) were from male subjects and 34% (29/86) were from female subjects. Furthermore, 69% (59/86) were from Caucasians, 1% (1/86) were from African Americans, 2% (2/86) were from Asian/Pacific Islanders, and 28% (24/86) were of other races. The left eye was treated in 51% (44/86) of the cases and the right eye was treated in 49% (42/86) of the cases. The mean age of the subjects treated was 41 years with a range from 23 to 66.

Table 1 presents demographic information for the all eyes treated.

Table 1:
Demographic Information
All Eyes (n=86)

Category	Classification	n	% Eyes
Gender	Male	57	66.3
	Female	29	33.7
Race	Caucasian	59	68.6
	African American	1	1.2
	American Indian/Aleut Eskimo	0	0.0
	Asian/Pacific Islander	2	2.3
	Other: Hispanic	24	27.9
Eyes	Right	42	48.8
	Left	44	51.2
CL History	None	83	96.5
	Soft	3	3.5
	RGP/PMMA	0	0.0
Age (in Years)	Average	41.3	
	Standard Deviation	± 10.8	
	Minimum	23	
	Maximum	66	

F. Data Analysis and Results

1. Preoperative Characteristics

Table 2 contains a summary of the preoperative manifest refractive error stratified by sphere and cylinder, expressed in plus cylinder notation.

Table 2
Pre-Operative Refractive Error* Stratified by Manifest Sphere and Cylinder (n=86)

	Cylinder									
	1 to ≤ 2 D		>2 to ≤ 3 D		>3 to ≤ 4 D		>4 to ≤ 5 D		Total	
Sphere	n	%	n	%	n	%	n	%	n	%
0 to ≤ –1 D	9	10.5	4	4.7	2	2.3	3	3.5	18	20.9
<–1 to ≤ –2 D	14	16.3	8	9.3	5	5.8	3	3.5	30	34.9
<–2 to ≤ –3 D	1	1.2	15	17.4	2	2.3	1	1.2	19	22.1
<–3 to ≤ –4 D	0	0.0	0	0.0	5	5.8	8	9.3	13	15.1
<–4 to ≤ –5 D	0	0.0	0	0.0	0	0.0	4	4.7	4	4.7
<-5 D	0	0.0	0	0.0	0	0.0	2	2.3	2	2.3
Total	24	27.9	27	31.4	14	16.3	21	24.4	86	100

**Refractions were measured at 8 feet; results shown are adjusted for optical infinity.*

All refractions were measured at 8 feet and adjusted to optical infinity (by subtracting 0.41 D from the spherical component of the refraction) for data analysis and presentation. After the refractions were adjusted, 15 of the 86 eyes were no longer classified as having mixed astigmatism because their sphere power shifted from hyperopic to myopic. Fourteen of these 15 eyes received a mixed astigmatism wavefront treatment pattern. One eye received a wavefront treatment pattern that was marginally classified as myopic astigmatism.

2. Postoperative Results

a. Patient Accountability

Of the 86 eyes treated, over 95% accountability was achieved at 1, 3 and 6-months, and 100% accountability was achieved at the point of stability, 3 months. Table 3 presents subject accountability over time.

Table 3
Subject Accountability
(N=86)

	1 Month		3 Months		6 Months		9 Months		12 Months	
	n	%	n	%	n	%	n	%	n	%
Available for Analysis	84	97.7	86	100.0	80	93.0	69	80.2	63	73.2
Discontinued^	0	0.0	0	0.0	2	2.3	6	7.0	6	7.0
Missed Visit	2	2.3	0	0.0	0	0.0	7	8.1	0	0.0
Not yet eligible	0	0.0	0	0.0	0	0.0	0	0.0	13	15.1
Lost to Follow-Up~	0	0.0	0	0.0	4	4.7	4	4.7	4	4.7
% Accountability*	**97.7%**		**100%**		**95.2%**		**86.3%**		**94.0%**	

^Eyes discontinued due to retreatment
~4 eyes were lost to follow-up due to the military deployment of 2 subjects during the follow-up of this study
*% Accountability=[Available for Analysis/(enrolled-discontinued-not yet eligible)] x 100

b. Stability of Outcome

Stability of outcome was evaluated for the cohort of eyes with a refraction at each visit through 9 months (n=67). Refractive stability was reached at 3 months and confirmed at 6 months. 100% of eyes with exams at 1, 3, 6 and 9 months post-operatively experienced a change in cylinder of ≤ 1.00 D between visits. Table 4 presents refractive stability of eyes with visits at 1, 3, 6, and 9 months post-operatively.

Table 4
Stability of Refractive Cylinder
Eyes that Underwent 1, 3, 6 and 9-Month Visits
(n=67)

	Between 1 and 3 Months	**Between 3 and 6 Months**	**Between 6 and 9 Months**
Change in Cylinder by ≤ 1.0 D	67	67	67
%	100	100	100
95% CI	95.6, 100	95.6, 100	95.6, 100
Mean Change in Cylinder ± SD	0.06	0.03	-0.02
95% CI	-0.01, 0.13	-0.02, 0.08	-0.07, 0.04

c. Effectiveness Outcomes

Eight-six (86) eyes of forty-four (44) subjects were enrolled and treated in this study Six (6) eyes underwent retreatment in this study (2 eyes after the 3-month visit and 4 eyes after the 6-month visit). All data for retreated eyes from exams completed prior to retreatment are included in all analyses.

Vector Analyses were conducted at the point of defined stability, 3-months.

1. Uncorrected Visual Acuity (UCVA)

All eyes were targeted to emmetropia. Visual acuity was measured at an 8-foot testing distance. The uncorrected visual acuity results presented in Table 5 exceed 90% 20/40 or better at all postoperative time points.

Table 5
UCVA* Over Time
(n=86)

	Pre-Op (n=86)	**1 Month (n=84)**	**3 Months (n=86)**	**6 Months (n=80)**	**9 Months (n=69)**	**12 Months (n=63)**
	n %	**n %**	**n %**	**n %**	**n %**	**n %**
	95% CI	**95% CI**	**95% CI**	**95% CI**	**95% CI**	**95% CI**
20/16 or better	0 0.0	17 20.2	20 23.3	20 25.0	18 26.1	26 41.3
	0.0, 3.4	12.3, 30.4	14.8, 33.6	16.0, 35.9	16.3, 38.1	29.0, 54.4
20/20 or better	0 0.0	56 66.7	53 61.6	48 60.0	51 73.9	47 74.6
	0.0, 3.4	55.5, 76.6	50.5, 71.9	48.4, 70.8	61.9, 83.7	62.1, 84.7
20/25 or better	0 0.0	71 84.5	72 83.7	68 85.0	60 87.0	55 87.3
	0.0, 3.4	75.0, 91.5	74.2, 90.8	75.3, 92.0	76.7, 93.9	76.5, 94.4
20/32 or better	0 0.0	77 91.7	79 91.9	75 93.8	68 98.6	61 96.8
	0.0, 3.4	83.6, 96.6	83.9, 96.7	86.0, 97.9	92.2, 100	89.0, 99.6
20/40 or better	12 14.0	79 94.0	82 95.3	77 96.3	68 98.6	61 96.8
	7.4, 23.1	86.7, 98.0	88.5, 98.7	89.4, 99.2	92.2, 100	89.0, 99.6
20/80 or better	59 68.6	83 98.8	85 98.8	79 98.8	69 100.0	63 100.0
	57.7, 78.2	93.5, 100	93.7, 100	93.2, 100	95.8, 100	95.4, 100
20/200 or better	86 100	84 100.0	86 100.0	80 100.0	69 100.0	63 100.0
	96.6, 100	96.5, 100	96.6, 100	96.3, 100	95.8, 100	95.4, 100
Worse than 20/200	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0	0 0.0
	0.0, 3.4	0.0, 3.5	0.0, 3.4	0.0, 3.7	0.0, 4.2	0.0, 4.6
Not reported	0	0	0	0	0	0
Total	86 100	84 100	86 100	80 100	69 100	63 100

* UCVA was measured at an 8-foot testing distance.

2. Accuracy

At 3 months post-operatively, 94.2% (81/86) of eyes were within 1.0 D of attempted sphere correction, and 88.4% (76/86) were within 1.0 D of attempted cylinder correction. Table 6a presents the accuracy of manifest sphere and cylinder over time, and table 6b presents the accuracy of WaveScan cylinder over time.

Table 6a
Accuracy of Sphere (to Zero) and Cylinder (to Zero) Component
(n=86)

	Pre-Op	**1 Month**	**3 Months**	**6 Months**	**9 Months**	**12 Months**
	N %	**n %**	**n %**	**n %**	**n %**	**n %**
	(95% CI)	**(95% CI)**	**(95% CI)**	**(95% CI)**	**(95% CI)**	**(95% CI)**
Manifest Sphere	**n=86**	**n=84**	**n=86**	**n=80**	**n=69**	**n=63**
± 0.50 D	0 0.0 0.0, 3.4	51 60.7 49.5, 71.2	57 66.3 55.3, 76.1	46 57.5 45.9, 68.5	44 63.8 51.3, 75.0	36 57.1 44.0, 69.5
± 1.00 D	18 20.9 12.9, 31.0	78 92.9 85.1, 97.3	81 94.2 87.0, 98.1	74 92.5 84.4, 97.2	63 91.3 82.0, 96.7	60 95.2 86.7, 99.0
Mean ± SD	-2.09 ± 1.12	-0.42 ± 0.44	-0.37 ± 0.42	-0.35 ± 0.50	-0.41 ± 0.44	-0.44 ± 0.38
Attempted		-2.10 ± 1.13	-2.10 ± 1.12	-1.99 ± 0.96	-1.98 ± 0.91	-1.93 ± 0.90
Achieved		-1.68 ± 1.15	-1.72 ± 1.19	-1.63 ± 1.02	-1.57 ± 0.91	-1.48 ± 1.01
% Achieved		73.6	76.7	81.3	78.7	70.2
Manifest Cylinder	**n=86**	**n=84**	**n=86**	**n=80**	**n=69**	**n=63**
± 0.50 D	0 0.0 0.0, 3.4	50 59.5 48.3, 70.1	51 59.3 48.2, 69.8	44 55.0 43.5, 66.2	41 59.4 46.9, 71.1	36 57.1 44.0, 69.5
± 1.00 D	1 1.2 0.0, 6.3	78 92.9 85.1, 97.3	76 88.4 79.7, 94.3	72 90.0 81.2, 95.6	62 89.9 80.2, 95.8	60 95.2 86.7, 99.0
Mean ± SD	2.98 ± 1.20	0.56 ± 0.49	0.61 ± 0.47	0.62 ± 0.42	0.59 ± 0.43	0.58 ± 0.43
Attempted		3.00 ± 1.20	2.98 ± 1.20	2.90 ± 1.15	2.89 ± 1.15	2.79 ± 1.13
Achieved		2.44 ± 1.13	2.37 ± 1.06	2.28 ± 1.01	2.30 ± 1.03	2.21 ± 1.00
% Achieved		80.5	79.3	78.3	79.1	79.2

Table 6b
Accuracy of WaveScan Cylinder (to Zero) Component
(n=86)

	Pre-Op		1 Month		3 Months		6 Months		9 Months		12 Months	
	N	%	n	%	n	%	n	%	n	%	n	%
	(95% CI)		(95% CI)		(95% CI)		(95% CI)		(95% CI)		(95% CI)	
WaveScan Cylinder	n=86		n=81		n=86		n=77		n=65		n=54	
± 0.50 D	0	0.0	23	28.4	20	23.3	22	28.6	18	27.7	15	27.8
± 1.00 D	0	0.0	57	70.4	64	74.4	58	75.3	47	72.3	42	77.8
± 2.00 D	21	24.4	80	98.8	86	100	76	98.7	65	100	53	98.2
Mean ± SD	3.04 ± 1.23		0.81 ± 0.44		0.81 ± 0.42		0.55 ± 0.43		0.80 ± 0.43		0.77 ± 0.42	
Attempted			3.01 ± 1.23		3.04 ± 1.23		2.93 ± 1.20		3.00 ± 1.19		2.75 ± 1.11	
Achieved			2.20 ± 1.09		2.23 ± 1.07		2.14 ± 1.03		2.20 ± 1.06		1.98 ± 0.99	
% Achieved			68.1		71.0		71.4		71.5		70.1	

3. Summary of Key Safety and Effectiveness Variables

Summaries of the key safety and effectiveness variables at Stability Endpoint of 3 Months stratified by pre-operative MRSE are presented in Table 7.

Table 7
Summary of Key Safety and Effectiveness Variables at Stability Endpoint of 3 Months *(Stratified by Pre-Operative MRSE)* (n=86)

Criteria	<-3.00 to -2.00 n/N, %		<-2.00 to -1.00 n/N, %		<-1.00 to 0.0 n/N, %		>0.0 to 1.0 n/N, %		>1.0 to 2.00 n/N, %		Cum Total n/N, %	
Effectiveness Variables												
N=86	n=4		n=26		n=34		n=18		n=4		N=86	
UCVA 20/20 or better†	3	75.0	16	61.5	19	55.9	11	61.1	4	100	53	61.6
UCVA 20/40 or better†	4	100	23	88.5	33	97.1	18	100	4	100	82	95.3
MRSE ± 0.50 D†	4	100	20	76.9	31	91.2	11	61.1	1	25.0	67	77.9
MRSE ± 1.00 D†	4	100	26	100	34	100	17	94.4	3	75.0	84	97.7
MRSE ± 2.00 D†	4	100	26	100	34	100	18	100	4	100	86	100
Cylinder ± 0.50 D	3	75.0	12	46.2	21	61.8	12	66.7	3	75.0	51	59.3
Cylinder ± 1.00 D	4	100	23	88.5	28	82.4	18	100	4	100	77	89.5
Cylinder ± 2.00 D	4	100	26	100	34	100	18	100	4	100	86	100
Safety Variables												
N=86	n=4		n=26		n=34		n=18		n=84		n=86	
Loss of ≥ 2 lines BSCVA*	0	0.0	0	0.0	0	0	0.0	0.0	0	0.0	0	0.0
Loss of > 2 lines BSCVA	0	0.0	0	0.0	0	0	0.0	0.0	0	0.0	0	0.0
BSCVA worse than 20/25	0	0.0	0	0.0	0	0	0.0	0.0	0	0.0	0	0.0
BSCVA worse than 20/40	0	0.0	0	0.0	0	0	0.0	0.0	0	0.0	0	0.0

† *UCVA and MRSE were measured at 8 feet; results shown are adjusted for optical infinity.*
* *One eye temporarily lost 2 lines of BSCVA at the 1 and 6 month visits (from 20/12.5 to 20/20). The acuity loss was associated with SPK and dryness, and the BSCVA returned to baseline by the 9-month visit when these conditions resolved.*

d. Higher Order Aberrations

Although the WaveScan WaveFront® System measures the refractive error and wavefront aberrations of the human eyes, including myopia, hyperopia, astigmatism, coma, spherical aberration, trefoil, and other higher order aberrations through sixth order, in the clinical study for this PMA, the average higher order aberration did not decrease after CustomVue™ treatment.

e. Safety Outcomes[1]

Adverse Events are summarized in Table 8. Overall, the device was deemed reasonably safe. The benchmark for each adverse event is a rate of less than 1 % per type of event. In addition to the 3 adverse events listed in the table below, one subject experienced an allergic reaction to a non-study systemic medication that required hospitalization 9 months post-operatively.

[1] Adverse Events and Complications outlined in the October 10, 1996 FDA Guidance Document for Refractive Surgery Lasers are included in Tables 8 and 9. Adverse Events are serious (sight or life-threatening) and unanticipated events; complications are anticipated, transient, and non-sight threatening sequelae to the surgery.

Table 8
Summary of Adverse Events
(n=86)

	<1 Month (n=86)		1 Month (n=84)		3 Months (n=86)		6 Months (n=80)		9 Months (n=69)		12 Months (n=63)	
	n	%	n	%	n	%	n	%	n	%	n	%
Corneal Infiltrate/Ulcer	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Corneal epithelial defect involving the keratectomy at 1 month or later	0	0	0	0.0	0	0.0	0	0.0	0	0.0	1^	1.6
Corneal edema at 1 month or later (specify "flap" or "bed" or both)	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Epithelium in the interface with loss of ≥2 lines of BSCVA	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Miscreated Flap	1†	1.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Melting of the flap (LASIK only)	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Uncontrolled IOP >10 mm Hg or any reading > 25 mm Hg	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Late onset of haze beyond 6 months with loss of 2 lines (10 letters) or more BSCVA	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Decrease in BSCVA of >10 letter not due to irregular astigmatism as shown by hard contact lens refraction, at 6 months or later	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Retinal Detachment	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Retinal Vascular Accidents	0	0.0	0	0.0	0	0	1‡	1.3	0	0.0	0	0.0

^An epithelial defect occurred when dendritic figures were cultured for herpes at >12 months post-op. The culture proved negative for herpes.
†One subject experienced a free LASIK cap during surgery. Although this event occurred on the day of surgery and resolved at the 3-month visit, it is reported in the <1-month column.
‡The subject experienced a branch retinal artery occlusion 8 months post-operatively that resolved with sequelae (hazy vision inferiorly) by the 9-month visit.

Complications that occurred during the clinical trial are summarized in Table 9.

Table 9
Summary of Complications
(n=86)

	<1 Month (n=86)		1 Month (n=84)		3 Months (n=86)		6 Months (n=80)		9 Months (n=69)		12 Months (n=63)	
	n	%	n	%	n	%	n	%	n	%	n	%
Misaligned flap	0	0.0	0	0.0	0	0.0	0.0	0.0	0	0.0	0	0.0
Corneal edema between 1 week and 1 month after the procedure	0	0.0	0	0.0	0	0.0	0.0	0.0	0	0.0	0	0.0
Peripheral corneal epithelial defect at 1 month or later	0	0.0	0	0.0	0	0.0	0.0	0.0	0	0.0	0	0.0
Epithelium in the interface	0	0.0	4^	4.8	4^	4.7	2	2.5	2	2.9	2	3.2
Foreign body sensation at 1 month or later	0	0.0	0	0.0	0	0.0	0.0	0.0	0	0.0	0	0.0
Pain at 1 month or later	0	0.0	0	0.0	0	0.0	0.0	0.0	0	0.0	0	0.0
Diplopia (ghost images) in the operative eye	0	0.0	3	3.6	7	8.1	4	5.0	2	2.9	4	6.3

^ 2eyes experienced epithelium in the interface 1 and 3-months post-retreatment.

Table 10 presents the results of the contrast sensitivity analysis pre-operatively and at 1, 3, 6 and 12-months post-operatively. A positive mean change reflects an improvement in contrast sensitivity.

Table 10
Contrast Sensitivity
(n=86)

	Pre-Op				Change from Pre-Op to 1 Months				Change from Pre-Op to 3 Months				Change from Pre-Op to 6 Months				Change from Pre-Op to 12 Months			
CPD	**3**	**6**	**12**	**18**	**3**	**6**	**12**	**18**	**3**	**6**	**12**	**18**	**3**	**6**	**12**	**18**	**3**	**6**	**12**	**18**
Dim w/ Glare	**n=86**				**n=84**				**n=86**				**n=80**				**n=63**			
Mean	1 51	1 45	0.86	0.44	0 00	0.03	0 08	0 07	-0.01	0.06	0.12	0.10	0.01	0.07	0.13	0.17	0.06	0 018	0.021	0 014
(SE)	0.024	0 037	0.038	0.039	0.024	0 034	0.038	0.039	0.025	0.039	0 034	0.036	0.025	0.041	0.038	0.045	0.026	0.043	0.050	0.050
P Value* ≤					0.953	0 456	0.050	0 093	0.740	0.114	**0.001**	**0.009**	0.622	0.108	**0.001**	**0.000**	**0.025**	**0.000**	**0.000**	**0.006**
Dim w/o Glare	**n=86**				**n=84**				**n=86**				**n=80**				**n=63**			
Mean	1 52	1 55	0.99	0 55	0.01	0 02	-0 01	0.02	0.03	0.03	0.11	0.12	0.08	0 09	0.11	0.12	0.08	0.13	0.18	0.18
(SE)	0 027	0 032	0 040	0.038	0 021	0.028	0.034	0.037	0.022	0.031	0.041	0.037	0.026	0.029	0.040	0.039	0 027	0 036	0 043	0.048
P Value* ≤					0 575	0 406	0 825	0.565	0 252	0.408	**0.007**	**0.002**	**0.002**	**0.002**	**0.006**	**0.004**	**0.005**	**0.001**	**0.000**	**0.000**
Bright w/o Glare	**n=86**				**n=84**				**n=86**				**n=80**				**n=63**			
Mean	1 72	1 88	1 47	0.99	0 01	0 00	0.05	0.05	0 04	0.07	0 06	0 08	0.02	0.06	0.09	0 08	0.04	0.08	0.12	0.13
(SE)	0 020	0 024	0.032	0.034	0 020	0.019	0.029	0 028	0.019	0.020	0.028	0 027	0.021	0.020	0.031	0.029	0.025	0.027	0.031	0 031
P Value* ≤					0.618	1.000	0.113	0.068	**0.042**	**0.001**	**0.040**	**0.003**	0.253	**0.005**	**0.004**	**0.007**	0 094	**0.006**	**0.000**	**0.000**

*Two tailed paired t test for the means.

Table 11 presents the number and percent of eyes with changes from baseline (>0.30 log units at 2 or more spatial frequencies) in contrast sensitivity at 3, 6 and 12-months post-operatively.

Table 11
Change in Contrast Sensitivity
(n=86)

	3 Months (N=86)			6 Months (N=80)			12 Months (N=63)		
	Decrease	No Change	Increase	Decrease	No Change	Increase	Decrease	No Change	Increase
Bright without Glare	3	75	8	3	68	9	1	55	7
%	3.5	87.2	9.3	3.8	85.0	11.3	1.6	87.3	11.1
Dim without Glare	6	64	16	4	58	18	3	40	20
%	7.0	74.4	18.6	5.0	72.5	22.5	4.8	63.5	31.7
Dim with Glare	4	67	15	4	63	13	3	37	23
%	4.7	77.9	17.4	5.0	78.8	16.3	4.8	58.7	36.5

f. Retreatment

Six eyes (6/86, 7.0%) underwent retreatment in this study.

g. Factors Associated with Outcomes

To evaluate the consistency of results and effect of treatment by study site and baseline characteristics, results at 3 months post-operatively were analyzed. The key safety and effectiveness variables were compared to target percentages to determine if the results were significantly different.

No eye had a BSCVA loss of > 2 lines and no eye had a BSCVA worse than 20/40, so there were no detectable differences between study sites and baseline characteristics relative to safety outcomes.

For each effectiveness criterion, comparisons between the actual and target outcomes (MRSE ± 0.50, MRSE ± 1.00, UCVA 20/40 or better) were made using a chi-square goodness-of-fit test. A Mantel-Haenszel one degree of freedom chi-square test was used to compare the observed percentages across categories. Those p-values are used to identify situations where there are differences between categories.

Specifically, the analyses of effect included: sex (female and male), race (white and other), investigational site (1, 2, 4, 5, 6, and 9), age group (<30, 30 to 39, 40 to 49, and ≥ 50), pre-operative contact lens use (None and Soft), pre-operative MRSE (< 2, 2 to <3, 3 to < 4, 4 to <5, and ≥ 5), laser room temperature (< 70°, 70°, 71°, 72° to

73°, 74°, and ≥ 75°), laser room humidity (< 30%, 30% to 35%, 36% to 40%, 41% to 45%, and > 45%), and surgeon.

In these analyses, statistically significant differences in outcomes were identified by comparing actual outcomes with FDA target values (MRSE ± 0.50 / 50%, MRSE ± 1.00 / 75%, UCVA 20/40 or better / 85%).

Throughout these analyses, there were six cases where the observed value did not meet the target value. For the outcome measure MRSE ± 0.50 D (target=50%), treatments in the pre-study MRSE group of >1.00 to 2.13 D had an observed value of 25%, and 25% was observed for surgeon Culbertson. For UCVA 20/40 or better (target = 85%), treatments in the age group of 40-49 had an observed value of 83%, treatments at site #9 and treatments by surgeon Maloney had an observed value of 83%, treatments conducted in a laser suite with a temperature of 71 degrees had an observed value of 75%.

Only one of these six values (25% for MRSE ± 0.5 D for pre-study MRSE >1.0 to 2.0) had a statistically significant difference from the target value. This group consisted of only 4 eyes.

All other subcategories met or exceeded the target value. Indeed, in many of these subcategories, the observed value was statistically significantly superior ($p < 0.05$) to the target value.

In addition to these analyses, outcomes were compared among the same categories (sex, race, site, age, pre-operative contact lens use, pre-operative MRSE, temperature, humidity and surgeon) for other effectiveness criteria (UCVA 20/20, Sphere ± 0.5 D, Sphere ± 1.0 D, Cylinder ± 0.5 D, Cylinder ± 1.0 D), with no pre-determined target values. Two cases of significant differences in outcomes were identified. A sex difference in percent of patients with UCVA 20/20 or better was significant (41% females, 72% males; p= 0.0062), as was the difference in percent with Cylinder ± 0.5 D (38% females, 70% males; p=0.0042).

h. Patient Satisfaction

Patients were asked to complete a questionnaire for each eye to evaluate vision pre-operatively and post-operatively. Upon completion of the questionnaire, both the patient and the investigator reviewed the form. To be included in the analysis, a pre-operative questionnaire had to have been completed. Patient questionnaire responses are presented pre-operatively and at 3 and 6 months post-operatively. Tables 12 and 13 presents a summary of patient satisfaction and patient symptoms.

Table 12:
Summary of Patient Satisfaction
All Eyes (n=86)

	Very Satisfied			Satisfied			Not Sure			Somewhat Dissatisfied			Very Dissatisfied			Not Reported		
	Pre n=86	3M n=86	6M n=80	Pre n=86	3M n=86	6M n=86	Pre n=86	3M n=86	6M n=80	Pre n=86	3M n=86	6M n=80	Pre n=86	3M n=86	6M n=80	Pre n=86	3M n=86	6M n=80
	n %	n %	n %	n %	n %	n %	n %	n %	n %	n %	n %	n %	n %	n %	n %	n %	n %	n %
Sharpness and Clarity	10	46	49	51	25	19	11	7	7	10	4	1	4	4	4	0	0	0
	11.6	53.5	61.3	59.3	29.1	23.8	12.8	8.1	8.8	11.6	4.7	1.3	4.7	4.7	5 0	0.0	0.0	0.0
Consistency of Vision	10	36	43	48	32	25	8	9	4	20	7	6	0	2	2	0	0	0
	11.6	41 9	53 8	55.8	37.2	31.3	9 3	10 5	5.0	23.3	8.1	7.5	0.0	2.3	2 5	0.0	0 0	0 0
Daylight Vision	11	49	41	53	25	33	10	0	0	12	9	2	0	3	4	0	0	0
	12.8	57.0	51 3	61.6	29.1	41 3	11.6	0.0	0.0	14 0	10.5	2.5	0.0	3.5	5 0	0 0	0.0	0 0
Night Vision	8	36	33	38	36	38	13	4	4	20	6	1	7	4	4	0	0	0
	9 3	41 9	41 3	44 2	41 9	47.5	15.1	4.7	5.0	23.3	7.0	1.3	8 1	4.7	5 0	0 0	0.0	0.0
Night Vision with Glare	5	28	31	28	40	30	21	9	13	22	5	2	10	4	4	0	0	0
	5 8	32.6	38 8	32.6	46.5	37 5	24.4	10.5	16 3	25.6	5.8	2.5	11.6	4.7	5.0	0.0	0.0	0.0

Table 13:
Summary of Patient Symptoms
All Eyes (n=86)

	Never			Rarely			Sometimes			Often			Always			Not Reported		
	Pre n=86	3M n=86	6M n=80	Pre n=86	3M n=86	6M n=86	Pre n=86	3M n=86	6M n=80	Pre n=86	3M n=86	6M n=80	Pre n=86	3M n=86	6M n=80	Pre n=86	3M n=86	6M n=80
	n %	n %	n %	n %	n %	n %	n %	n %	n %	n %	n %	n %	n %	n %	n %	n %	n %	n %
Dryness	30	10	8	24	30	28	27	27	30	5	16	14	0	3	0	0	0	0
	34.9	11 6	10.0	27 9	34.9	35 0	31 4	31 4	37 5	5.8	18.6	17.5	0 0	3 5	0.0	0 0	0 0	0.0
Blurry Vision	16	13	19	31	32	34	25	29	20	7	6	3	7	6	4	0	0	0
	18 6	15 1	23.8	36 0	37.2	42.5	29.1	33.7	25.0	8 1	7.0	3.8	8 1	7.0	5.0	0.0	0 0	0.0
Fluctuation of vision	25	25	31	34	29	24	19	29	21	8	3	4	0	0	0	0	0	0
	29 1	29 1	38 8	39.5	33.7	30.0	22 1	33.7	26 3	9 3	3.5	5.0	0.0	0.0	0.0	0.0	0.0	0.0
Glare	21	32	33	32	32	25	26	20	21	3	0	0	4	2	1	0	0	0
	24 4	37 2	41.3	37.2	37.2	31.3	30.2	23 3	26.3	3.5	0.0	0.0	4.7	2.3	1.3	0 0	0.0	0.0
Halos Around Lights	25	30	34	21	29	22	29	10	13	5	10	7	6	7	4	0	0	0
	29.1	34.9	42.5	24.4	33.7	27.5	33 7	11.6	16.3	5.8	11.6	8.8	7.0	8.1	5.0	0.0	0.0	0.0
Difficulty at Night W/Glare	8	30	33	35	39	35	29	8	5	10	3	3	4	6	4	0	0	0
	9 3	34 9	41.3	40 7	45.3	43.8	33.7	9.3	6.3	11.6	3.5	3.8	4.7	7.0	5.0	0.0	0.0	0.0
Ghost or Double Images	53	63	60	14	8	12	12	13	3	6	0	1	0	2	4	1	0	0
	62.4	73 3	75 0	16 5	9.3	15.0	14.1	15.1	3.8	7.1	0.0	1.3	0 0	2.3	5 0	1 2	0.0	0 0

i. Device Failures

There were no device failures reported for this study for the indication of mixed astigmatism. However, there was one device failure, previously reported at one center during the treatment period under PMA supplement P930016/S017, for the study of hyperopic astigmatism.

XI. CONCLUSIONS DRAWN FROM THE STUDIES

Preclinical studies completed for this device did not raise any new safety or effectiveness concerns. Clinical studies demonstrated that safety and effectiveness parameters fell within acceptable FDA criteria providing reasonable assurance that the device is safe and effective, when used in accordance with the directions for use, for wavefront-guided LASIK treatment with the VISX STAR S4 IR™ Excimer Laser System with Variable Spot Scanning and WaveScan® derived ablation targets for the correction of mixed astigmatism.

XII. PANEL RECOMMENDATION

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Ophthalmic Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CDRH DECISION

CDRH issued an approval order on

The applicant's manufacturing facility was inspected and found to be in compliance with the Quality System Regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

- Postapproval Requirements and Restrictions: see Approval Order.
- Hazards to Health from Use of the Device: see Indications, Contraindications, Warnings, Precautions, and Adverse Events in the labeling.
- Directions for use: see labeling.